REMARKS

A check for the fee for a four month extension of time accompanies this response. Any fees that may be due in connection with filing this paper or with this application may be charged to Deposit Account No. 06-1050. If a Petition for Extension of time is needed, this paper is to be considered such Petition. A change in Power of Attorney to the undersigned was previously filed.

Specification

Amendments to the specification made herein correct minor obvious typographical, formatting, and grammatical errors. In addition, the language in Example 4 (see *e.g.* page 45) and Example 8 (see *e.g.* page 49) relating to exemplary assays using TNF/TNFR is amended from the past tense to recite the present tense. As noted in the Information Disclosure Statement, filed under separate cover, this error was inadvertent. No new matter is added.

Claims

Claims 1-7, 9, 11-16, 45-48, 50-54, 56-66 are pending in this application. All claims, including claims to non-elected subject matter, are retained herein pending reconsideration of the restriction requirement. Applicant reserves the right to file divisional and continuation applications to non-elected subject matter. Claims 1, 7, 9, 12-16, 46, 50, 53, 54, 56, 59, and 62-66 are amended herein to correct minor typographical, formatting, grammatical and spelling errors and to clarify the claimed subject matter. Claim 12 and claim 56 are amended to change the claim dependency to correct antecedent basis. No new matter is added.

Traversal of the Requirement for Restriction

The requirement for restriction as set forth is traversed. Applicant respectfully requests reconsideration of the restriction as between and among Groups I-IV. The Examiner contends that the methods are unrelated as they allegedly are drawn to different methods comprising different components and/or method steps. Applicant respectfully disagrees insofar as the methods contain related subject matter. In this instance, each of Groups I-IV contain overlapping subject matter.

Group I

Independent claim 1 (and dependent claims 2-7, 11-16, 45-48, and 50-52) is directed to a method of identifying a modified mammalian protease that cleaves a substrate sequence in a target protein by recited steps. The target protein is selected from among a cell surface molecule that transmits an extracellular signal for cell proliferation, a cytokine, a cytokine

receptor, and a signaling protein that regulates apoptosis. The protease is not specified. The recited steps are:

> (a) producing a library of mutein protease sequences, each different mutein protease sequence in the library being a member of the library, each member having N mutations relative to a wild-type scaffold sequence of a mammalian protease wherein N is a positive integer,
> (b) measuring an activity of at least two members of the library in cleaving the substrate sequence, and
> (c) identifying at least one mutein protease having an increased cleavage activity and/or altered specificity for cleaving said substrate sequence, relative to the wild-type scaffold sequence.

Dependent claim 7 sets forth a list of proteases, including granzyme B. Dependent claim 12 sets forth that the target protein is caspases-3, VEGF, or VEGFR-R. Dependent claim 16 sets forth additional steps of the method as follows:

> (d) providing two or more members of the protease library identified with increased cleavage activity and/or altered specificity,
> (e) combining the mutations on a first mutein protease with the mutations on a second mutein protease to produce a third mutein protease; and
> (f) identifying whether the combination produces a combined specificity protease that has increased cleavage activity and/or altered specificity in regards to the substrate sequence.

Group II

Independent claim 53 (and its dependents 54, and 56-58) also is directed to a method of identifying a modified mammalian protease that cleaves a substrate sequence in a target protein by recited steps. The mammalian protease is set forth among a group of listed proteases, including granzyme B. The recited methods steps are the recited method steps (a)-(f) set forth in Group I above. The target protein is not specified.

Group III

Independent claim 59 (and its dependents 60-62) is directed to a method of identifying a modified human protease that cleaves a substrate sequence in a target protein by recited steps, where the target protein is selected from among the same target proteins set forth in Group I. The claim specifies that the target protein is involved with a pathology in a human. The recited method steps are the same recited method steps (a)- (c) in Group I, except that step (a) specifies that the protease is selected from among a list of proteases, including granzyme B. Dependent claim 62 specifies that the target protein is selected from a list of proteins, including caspases 3.

Group IV

Independent claim 63 (and its dependents 64-66) is directed to a method of identifying a modified human protease that cleaves a substrate sequence in a target protein by recited steps. The recited steps are the same as steps (a)- (c) in Group I, except step (a) sets forth a list of proteases, including granzyme B; and step (b) sets forth a list of target proteins, including caspases 3.

Hence, each of Groups I-IV are directed to a method of identifying a modified protease by the same recited steps. Groups I and II are directed to a method of identifying a modified mammalian protease, which includes a human protease. Groups III and IV are directed to a method of identifying a modified human protease. The claims in each of Groups I-IV specify the protease that is used in the recited methods from among a list of proteases. Although the list of proteases is not identical among each of the groups, it is overlapping in subject matter. For example, each of Groups I-IV specify that the protease can be granzyme B. Likewise, the claims in each of Groups I, III, and IV specify the target protein that is used in the recited methods from among a list of target proteins. Although the list of target proteins is not identical among each of the groups, it is overlapping in subject matter. For example, each of Groups I, III and IV specify that the target protein can be caspase 3. Thus, although the subject matter of Groups I-IV is not identical, the claimed subject matter is related because the claims overlap.

The presence of overlapping subject matter among the claims of Groups I-IV is apparent given that all of the groups read on the elected species of a granzyme B protease and the elected species of a caspase 3 target protein. Thus, each of claims 1, 53, 59, and 63 of Groups I-IV, respectively, encompass subject matter of the elected species. Thus, claims in Groups I-IV are related, insofar as they contain overlapping subject matter.

The Examiner is reminded of the cautionary language in MPEP §806, paragraph 3, which states:

> [w]here inventions are related as disclosed but are not distinct as claimed, restriction is never proper. Where restriction is required by the Office [obviousness-type] double patenting cannot be held, and thus, it is imperative the requirement should never be made where related inventions as claimed are not distinct.

See, also MPEP §804.01, which states:

> 35 U.S.C. §121 authorizes the Commissioner to restrict the claims in a patent application to a single invention when independent and distinct

> inventions are presented for examination. The third sentence of 35 U.S.C. §121 prohibits the use of a patent issuing on an application with respect to which a requirement for restriction has been made, or on an application filed as a result of such a requirement, as a reference against any divisional application, if the divisional application is filed before the issuance of the patent. The 35 U.S.C. §121 prohibition applies only where the Office has made a requirement for restriction. The prohibition does not apply where the divisional application was voluntarily filed by the applicant and not in response to an Office requirement for restriction. This apparent nullification of double patenting as a ground of rejection or invalidity in such cases imposes a heavy burden on the Office to guard against erroneous requirements for restriction where the claims define essentially the same invention in different language and which, if acquiesced in, might result in the issuance of several patents for the same invention.

Where restriction is maintained, the Office is reminded that obviousness-type double patenting cannot be made between applications containing subject matter directed to the restricted groups. The consequence of the overlap in the groups could result in the issuance of patents with claims to overlapping subject matter in which the Office would be precluded from holding obviousness-type double patenting.

If the claims are restricted into these four groups, Applicant ultimately could be granted four patents that expire on different days and/or are not required to be commonly owned, containing overlapping claims. For example, if claim 63 in Group IV issued first containing a claim to the elected species of a granzyme B protease and a caspase 3 target protein, obviousness-type double patenting could not be held as between any of the claims, including claims 1, 53 and 59, of any of Groups I-III, in later issuing divisional applications. As noted claims in all of Groups I-IV read on the elected species. The Office, however, will be precluded from rejecting any of these claims based on obviousness-type double patenting over a claim to the elected species.

Hence, if the restriction requirement as between Groups I-IV is maintained, the Office is precluded from rejecting any of the claims in any of Groups I-III over any of the claims or subject matter of Group IV. Therefore, the requirement for restriction among Groups I-IV is incorrect. Reconsideration of the requirement for restriction among Groups I-IV respectfully is requested.

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Entry of this amendment and examination of the application are respectfully requested.

Respectfully submitted,

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